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Anaphylactic Reaction Induced by Diclofenac: A Case Report

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Abstract: An anaphylactic reaction is a most severe immune-mediated reaction. Diclofenac is a widely used non-steroidal anti-inflammatory drug (NSAID) derivative of phenylacetic acid, and continues to be routinely prescribed. We report a case of an anaphylactic reaction induced by oral diclofenac.

Key words: Allergic reaction, Anaphylactic reaction, Diclofenac

Introduction

Diclofenac is a widely used non-steroidal anti-inflammatory drug (NSAID) derivative of phenylacetic acid, and continues to be routinely prescribed. Diclofenac is considered to be safe, and anaphylactic reactions to diclofenac are rare. We report a case of an anaphylactic reaction induced by oral diclofenac.

Case Report

A 45-year-old, 65 kilogram, 170 centimeter male patient was scheduled for dental implants of 25 and 26 under sedation. He had frequently undergone previous dental procedures without complication. He was previously administered diclofenac on several occasions for recurrent pharyngitis. His personal and family history for atopic diseases was negative. He had no previous history of a drug allergy.

After 30 minutes of uneventful surgery, oral diclofenac (25 mg) was administered. Within 15 minutes after oral diclofenac sodium administration, urticaria developed on the face, both arms, and legs, spreading later to the entire body (Fig. 1), suggesting an allergic onset. At the same time, there was a marked decrease in Spo_2 (93%) despite the administration of 6 liters per minute of oxygen with a facemask, and the blood pressure was 85/45 mmHg with mild tachycardia (110 bpm). All of these symptoms were relieved by the immediate subcutaneous injection of 0.3 mg adrenaline. Moreover 1,500 ml of lactated Ringer's solution, 500mg methylprednisolone and 40mg chlopheniramine were administered intravenously. Oxygen saturation never dropped below 93%, and bronchospasm did not occur. When hemodynamic stability was restored, generalized urticaria became apparent. Within 6 hours after treatment, the urticarial rash had disappeared and it was suggested that he contact an allergy specialist.

Six weeks later, with the patient's consent, cutaneous tests to latex and to all drugs (lidocaine, midazolam, flumazenil, and diclofenac) used during surgery were performed. A prick test with diclofenac sodium was positive, whereas cutaneous tests to latex and to all other drugs were negative. To confirm that diclofenac sodium was the causative agent, an *in vitro* leukocyte histamine release assay[1] was performed with diclofenac, which yielded positive results (histamine release

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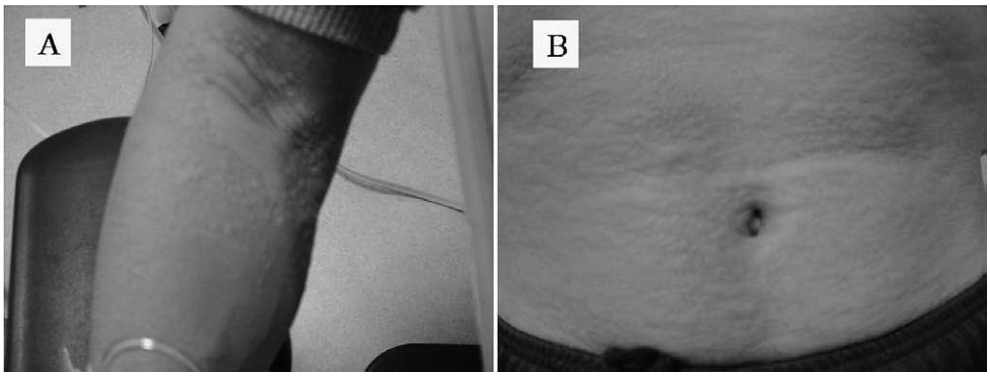

Fig. 1 Severe urticarial rash of A, medial elbow and B, abdomen.

of more than 5%), whereas it remained negative in control serum.

Discussion

Allergic reactions are among the more common emergencies seen in dentistry. A survey of 4,309 dentists in North America reported a total of 30,602 emergency events, including 304 involving anaphylactic reaction[2,3]. Malamed described penicillins, sulfonamides, aspirin, esters, parabens, metasulfites, and latex as common allergens in dentistry[3].

Diclofenac is considered to be safe, with a worldwide administration to 7.6 million patients per year[4]. Van der Klauw *et al*[5]. identified only 30 cases of probable anaphylaxis to diclofenac sodium in 992 reports on drug reactions. Anaphylactic reactions to diclofenac sodium are rare[6]. We herein report a case of allergic reaction to diclofenac in an adult who developed an itching sensation, urticarial rash, mild hypotension, and blood oxygen desaturation following oral diclofenac administration that necessitated immediate intervention. Although blood sampling for tryptase levels was not performed because the patient frequently received uneventful dental treatment, we tend to regard this reaction to be most probably anaphylactic, based on a positive prick test and leukocyte histamine release assay.

The first choice of treatment for an anaphylactic reaction is adrenaline. Unfortunately, the correct dosage and route for administration of adrenaline have been a source of confusion and conflict in medical literature[7]. Many authors conclude that the use of intravenous adrenaline is too dangerous and rarely, if ever, justified, as it causes severe complications such as cardiac arrhythmias, myocardial ischemia, and severe hypertension[7,8]. Therefore, we performed subcutaneous injection to prevent such complications. Corticosteroids and antihistamines could be used in conjunction with adrenaline to help reduce the overall duration of the reaction and may prevent a relapse[7,9]. However, these drugs should never be used to the exclusion of adrenaline in the management of anaphylactic reactions[9].

An anaphylactic reaction usually manifests immediately after the administration of an allergen. In rare cases, it may be delayed for a few hours[10], or even be biphasic[11]. Early symptoms include a sensation of warmth, itching, and a feeling of anxiety and panic[9]. These may progress into an erythematous or urticarial rash. A severe state may lead to acute, irreversible asthma, laryngeal edema, cardiac dysfunction, arrhythmias and even cardiac arrest[9]. The symptoms in the presented case remained in the early state. The prompt recognition and treatment of the anaphylactic reaction probably prevented progression to a severe state.

In summary, we report a case of an anaphylactic reaction induced by oral diclofenac. All dentists should note that even with a considerably safe drug such as diclofenac, a severe anaphylactic event may be induced, and appropriate actions need to be carried out immediately possible to save the patient's life.

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References

1. Vervloet D., Arnaud A., Vellieux P., Kaplanski S., and Charpin J.: Anaphylactic reactions to muscle relaxants under general anesthesia. J Allergy Clin Immunol 63: 348-353, 1979.
2. Malamed S.F.: Managing medical emergencies. J Am Dent Assoc 124: 40-53, 1993.
3. Malamed S.F.: Emergency medicine: beyond the basics. J Am Dent Assoc 128: 843-854, 1997.
4. O'Brien W.M.: Adverse reactions to nonsteroidal anti-inflammatory drugs. Diclofenac compared with other nonsteroidal anti-inflammatory drugs. Am J Med 28: 70-80, 1986.
5. Van der Klauw M.M., Wilson J.H., and Stricker B.H.: Drug-associated anaphylaxis: 20 years of reporting in the Netherland (1974-1994) and review of literature. Clin Exp Allergy 26: 1355-1363, 1996.
6. Hadar A., Holcberg G., and Mazor M.: Anaphylactic shock after diclofenac sodium (Voltaren). Harefuah 138: 211-212, 2000.
7. Brown A.F.: Anaphylactic shock: mechanisms and treatment. J Accid Emerg Med 12: 89-100, 1995.
8. Lip G.Y., and Metcalfe M.J.: Adrenaline in allergic emergencies. BMJ 8: 366-367, 1992.
9. Ogunsalu C.O.: Anaphylactic reaction following administration of lignocaine hydrochloride infiltration. Aust Dent J 43: 170-171, 1998.
10. Fisher M.M.: Clinical observations on the pathophysiology and treatment of anaphylactic cardiovascular collapse. Anaesth Intensive Care 14: 17-21, 1986.
11. Douglas D.M., Sukenick E., Andrade W.P., and Brown J.S.: Biphasic systemic anaphylaxis: an inpatient and outpatient study. J Allergy Clin Immunol 93: 977-985, 1994.